In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Please amend claims 78-81 and 93-102 as indicated.

Please add new claims 106-116 as follows:

Status of Claims

Claims 1-42 **(Cancelled)**

Claim 43 **(Withdrawn)** A method for specifically cleaving a preselected RNA comprising contacting said RNA with an oligomeric compound comprising at least twelve ribofuranosyl nucleoside subunits in a sequence which is specifically hybridizable with said preselected RNA;

said nucleoside subunits being joined by internucleoside bonds which are more stable to degradation as compared to phosphodiester bonds;

the compound having at least one modified nucleoside subunit, which modified nucleoside subunit is modified to improve at least one of: pharmacokinetic binding, absorption, distribution or clearance properties of the compound; affinity or specificity of said compound to said target RNA; or modification of the charge of said compound as compared to an unmodified compound; and

said compound having at least four consecutive 2'-hydroxyl ribonucleoside subunits.

Claim 44 **(Withdrawn)** The method of claim 43 wherein said compound has at least five consecutive ribonucleoside subunits.

Claim 45 **(Withdrawn)** A method for treating an organism having a disease comprising contacting the organism with an oligomeric compound having a sequence of nucleoside subunits capable of specifically hybridizing with a complementary strand of ribonucleic acid with at least one

of the nucleoside subunits being modified to improve at least one of: pharmacokinetic binding, absorption, distribution or clearance properties of the compound; affinity or specificity of said compound to said target RNA; or modification of the charge of said compound as compared to unmodified compound; and a plurality of the nucleoside subunits being located in a consecutive sequence and having 2'-hydroxyl-pentofuranosyl sugar moieties.

Claim 46 **(Withdrawn)** A composition including a pharmaceutically effective amount of an oligomeric compound in a pharmaceutically acceptable diluent or carrier, said oligomeric compound comprising a sequence of nucleoside subunits capable of specifically hybridizing with a complementary strand of RNA wherein a plurality of the nucleoside subunits of the oligomeric compound are modified to improve at least one of: pharmacokinetic binding, absorption, distribution or clearance properties of the compound; affinity or specificity of said compound to said target RNA; or modification of the charge of said compound as compared to an unmodified compound; and wherein a further plurality of the nucleoside subunits have 2'-hydroxyl-pentofuranosyl sugar moieties.

Claims 47-67 **(Cancelled)**

Claim 68 **(Withdrawn)** A mammalian ribonuclease having the activity of catalyzing the degradation of a double stranded substrate wherein one of said strands of said substrate is a RNA and the other of said strands of said substrate comprises a compound having a plurality of 2' modified nucleoside subunits and at least four consecutive ribofuranosyl nucleoside subunits having 2'-hydroxyl moieties thereon.

Claim 69 **(Withdrawn)** A mammalian ribonuclease of claim 68 wherein said subunits are joined by phosphorothioate internucleoside linkages or phosphodiester internucleoside linkages.

Claim 70 **(Withdrawn)** A mammalian ribonuclease of claim 68 wherein a portion of said subunits are joined by phosphorothioate internucleoside linkages.

Claim 71 **(Withdrawn)** A mammalian ribonuclease of claim 70 wherein said subunits are joined by phosphodiester internucleoside linkages.

Claim 72 **(Withdrawn)** A mammalian ribonuclease of claim 70 wherein all of said subunits are joined by phosphorothioate internucleoside linkages.

Claim 73 **(Withdrawn)** A mammalian ribonuclease of claim 68 wherein at least some of said subunits are 2'-O-alkyl nucleoside subunits.

Claim 74 **(Withdrawn)** A mammalian ribonuclease having the activity of catalyzing the degradation of a double stranded substrate wherein: said activity is inhibited by NaCl; said activity requires Mg^{++}; and said mammalian ribonuclease has an apparent molecular weight, as determined by SDS-PAGE, of about 50 to about 80 kilodaltons.

Claim 75 **(Withdrawn)** A mammalian ribonuclease of claim 74, wherein said ribonuclease is isolated from nuclei.

Claim 76 **(Withdrawn)** A mammalian ribonuclease of claim 74, wherein said ribonuclease is isolated from cytosol.

Claim 77 **(Withdrawn)** The mammalian ribonuclease of claim 74, wherein said ribonuclease is isolatable from human cells or tissues.

Claim 78 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein said first and said second oligonucleotides each have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said duplex; at least one of said first and said second oligonucleotides having ~~have~~ portions flanking said central portions having chemical modifications which make them resistant to single-stranded nucleases.

Claim 79 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein said first and said second oligonucleotide each have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said duplex; at least one of said first and said second oligonucleotides having ~~have~~ portions flanking said central portions having chemical modifications which make them resistant to single-stranded nucleases and increase their affinity for the other oligonucleotide of the duplex.

Claim 80 **(Currently Amended)** ~~A~~ The double-stranded RNA enzyme substrate of claim 78, wherein said chemical modifications are phosphorothioate linkages or 2'-methoxy modifications.

Claim 81 **(Currently Amended)** An affinity matrix comprising the ~~dsRNA~~ double-stranded RNA enzyme substrate of claim 78.

Claim 82 **(Withdrawn)** A method of purifying a ribonuclease or non-degradative RNA-binding protein comprising contacting a sample containing said ribonuclease or non-degradative RNA-binding protein with the affinity matrix of claim 81.

Claims 83-88 **(Cancelled)**

Claim 89 **(Withdrawn)** Use of said ribonuclease of claim 74 for treating an organism having a disease characterized by the undesired production of a protein encoded by a mRNA.

Claim 90 **(Withdrawn)** Use of said ribonuclease of claim 74 for identifying one of a mRNA or a protein encoded by said mRNA.

Claim 91 **(Withdrawn)** Use of said ribonuclease of claim 74 for diagnosing an aberrant state in an organism associated with a protein encoded by a mRNA.

Claim 92 **(Withdrawn)** A mammalian ribonuclease having the activity of catalyzing the degradation of a double stranded substrate wherein one of said strands of said substrate is a RNA and the other of said strands comprises a compound having chemical modifications that are resistant to single-stranded nucleases or increase affinity for the other strand of the substrate.

Claim 93 **(Currently Amended)** A double-stranded RNA enzyme substrate of claim 78, wherein one of said oligonucleotides has the nucleotide sequence of SEQ ID NO:8.

Claim 94 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages and wherein said portions are base-paired with each other in said duplex.

Claim 95 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion having at least four consecutive ribofuranosyl residues that

are base-paired with each other in said duplex; and at least one of said first and said second oligonucleotides including ~~include~~ a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases.

Claim 96 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion that ~~are~~ is base-paired with each other in said duplex; and at least one of said first and said second oligonucleotides ~~have~~ having a further portion that includes a chemical modification that increases the affinity of said oligonucleotide for the other oligonucleotide.

Claim 97 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion having at least four consecutive ribofuranosyl residues and where said portions are base paired with each other in said duplex; and at least one of said first and second oligonucleotides ~~include~~ includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases and that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

Claim 98 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein at least one of said first and said second oligonucleotides includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases and that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

Claim 99 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein at least one of said first and

said second oligonucleotides includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases.

Claim 100 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein at least one of said first and said second oligonucleotides includes a chemical modification that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

Claim 101 **(Currently Amended)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein said first and said second oligonucleotides each include a portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said portions are base-paired with each other in said duplex, and wherein one of said first and said second oligonucleotides ~~comprising~~ comprises from eight to fifty nucleoside subunits.

Claim 102 **(Currently Amended)** The double-stranded RNA enzyme substrate of claim 101 wherein said one of said first and said second oligonucleotides comprises from twelve to thirty subunits.

Claim 103 **(Withdrawn)** A mammalian ribonuclease having the activity of catalyzing the degradation of a double stranded substrate, wherein one of said strands of said substrate is a RNA and the other of said strands of said substrate comprises a compound having at least four consecutive ribofuranosyl nucleoside subunits having 2'-hydroxyl moieties thereon.

Claim 104 **(Withdrawn)** The mammalian ribonuclease of claim 103 wherein the other of said strands comprises a compound having from eight to fifty subunits.

Claim 105 **(Withdrawn)** The mammalian ribonuclease of claim 103 wherein the other of said strands comprises a compound having from twelve to thirty subunits.

Claim 106 **(New)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein said first and said second oligonucleotides have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said duplex; at least one of said first and said second oligonucleotides having portions flanking said central portions, said portions having chemical modifications which make them resistant to single-stranded nucleases, and wherein one of said oligonucleotides has the nucleotide sequence of SEQ ID NO:8.

Claim 107 **(New)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein said first and said second oligonucleotides are separate strands, each of said first and second oligonucleotides having a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said duplex; at least one of said first and said second oligonucleotides having portions flanking said central portions having chemical modifications which make them resistant to single-stranded nucleases.

Claim 108 **(New)** The double-stranded RNA enzyme substrate of claim 107 wherein said chemical modifications increase the affinity of said oligonucleotide for the other oligonucleotide of the duplex.

Claim 109 **(New)** A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides are separate strands, each of said first and second oligonucleotides including a

portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages and wherein said portions are base-paired with each other in said duplex.

Claim 110 (New) A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides are separate strands, each of said first and second oligonucleotides including a portion having at least four consecutive ribofuranosyl residues that are base-paired with each other in said duplex; and at least one of said first and said second oligonucleotides including a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases.

Claim 111 (New) A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides are separate strands, each of said first and second oligonucleotides including a portion that ~~are~~ is base-paired with each other in said duplex; and at least one of said first and said second oligonucleotides having a further portion that includes a chemical modification that increases the affinity of said oligonucleotide for the other oligonucleotide.

Claim 112 (New) A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides are separate strands, each of said first and second oligonucleotides including a portion having at least four consecutive ribofuranosyl residues and where said portions are base paired with each other in said duplex; and at least one of said first and second oligonucleotides including a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases and that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

Claim 113 (New) A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides are separate strands, and wherein at least one of said first and said second oligonucleotides includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases.

Claim 114 (New) The double-stranded RNA enzyme substrate of claim 113 wherein said chemical modification the affinity of said oligonucleotide for the other of said oligonucleotides.

Claim 115 (New) A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides are separate strands, and wherein at least one of said first and said second oligonucleotides includes a chemical modification that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

Claim 116 (New) A double-stranded RNA enzyme substrate comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein said first and said second oligonucleotides are separate strands, each of said first and second oligonucleotides including a portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said portions are base-paired with each other in said duplex, and wherein one of said first and said second oligonucleotides comprises from eight to fifty nucleoside subunits.